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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,533	12/29/2000	Stephen M. Coutts	252312005704	1380
25226 7590 05/29/2007 MORRISON & FOERSTER LLP 755 PAGE MILL RD PALO ALTO, CA 94304-1018			EXAMINER LUKTON, DAVID	
			ART UNIT 1654	PAPER NUMBER
			MAIL DATE 05/29/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/752,533	<b>Applicant(s)</b> COUTTS ET AL.	
	<b>Examiner</b> David Lukton	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.  
4a) Of the above claim(s) 129 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Continuation of Disposition of Claims: Claims pending in the application are 22,23,26,32,35,36,43,45,46,51-54,64-77,79-82,84,86,89,99-111,113-125,128-144 and 146-168.

Continuation of Disposition of Claims: Claims rejected are 22,23,26,32,35,36,43,45,46,51-54,64-77,79-82,84,86,89,99-111,113-125,128,130-144 and 146-168.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/28/07 has been entered.

Pursuant to the directives of the response filed 2/28/07, several claims have been amended. Claims 22, 23, 26, 32, 35, 36, 43, 45, 46, 51-54, 64-77, 79-82, 84, 86, 89, 99-111 113-125, 128-144, 146-168 remain pending.

Claims 22, 23, 26, 32, 35, 36, 43, 45, 46, 51-54, 64-77, 79-82, 84, 86, 89, 99-111, 113-125, 128, 130-144, 146-168 are examined in this Office action; claim 129 remains withdrawn from consideration.

Applicants' arguments filed 2/28/07 have been considered and found not persuasive. The "ODP" rejection over USP 5,552,391 is withdrawn in view of the terminal disclaimer.

. . . . .

The abbreviations "**VPM**", "**BAM**" and "**PEG**" are as defined previously.

✦

Claims 22, 64 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. USP 5,276,013 or claim 1 of U.S. Patent No. USP 6,060,056. Applicants have acknowledged the

existence of these rejections, but have added no new arguments. Accordingly, the rejections are maintained without further comment.

. . . . .

Claims 22, 64 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 and 32 of U.S. Serial No. 09/753350; claims 22, 64, 78 and 80 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 96 of U.S. Serial No. 10/867,874. Applicants have acknowledged the existence of these rejections, but have added no new arguments. Accordingly, the rejections are maintained without further comment.

✦

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22, 23, 26, 32, 35, 36, 43, 45, 46, 51-54, 64-77, 79-82, 84, 86, 89, 99-111, 113-125, 128, 130-144, 146-168 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Descriptive support is lacking for the claimed invention.

Claim 22 requires, among other things, that the VPM have at least two branching groups, and those two branching groups give rise to 4 or more attachment sites. As it happens, there is no descriptive support for this, even by itself, but even if such support existed, there would still remain the matter of the two branching groups / 4 attachment sites **in conjunction with** the other selections. In addition to the foregoing, claim 22 implies that with just two branching groups, one could have, e.g., 10 or 15 different attachment sites (this conclusion is reached because the number "10" is greater than the number "4"). There is no description of this situation either. That is, claim 22 permits the number of "attachment sites" to vary without limit, for the case of just two branching groups.

Possibly it is true that any one of the features (taken by itself) of the claimed genus can be found in the specification. Even if this is true, the more important issue is that what applicants have done is to "pick and choose" limitations from a myriad of possibilities. This process of "picking and choosing", as well as any subgenus resulting from this process, constitutes new matter.

Thus, in presenting the instant claims, applicants have started with formula 2 (page 4, specification), arbitrarily selected substituents for each of  $L^{[2]}$ ,  $J^{[2]}$ ,  $Z^{[2]}$  and  $T^{[2]}$ , combined them in a manner that has not been described, permitted the product of  $p[2]$  and  $n[2]$  to vary independently of  $n[2]$ , and combined the foregoing with limited a subgenus for  $G^{[2]}$ .

In addition to the foregoing, there is the matter of a description of "how to make" the claimed compounds by the prescribed route (other than the species depicted in the reaction schemes). The examiner does not argue that the organic chemist of ordinary skill, upon being presented with a specific structure that falls within the scope of the claimed invention, would (necessarily) be unable to synthesize the compound that is represented by the specific structure. Instead, the issue concerns that of "how to make" compounds (other than the species depicted in the reaction schemes) by conjugating the specific (required) "VPM" first with the linker and then with the "BAM". It is noted that on page 11, line 15+ there is a general description of the underlying concept. In addition, there is a discussion on page 22, line 29 to page 26, line 5 regarding the case of the "BAM" being a polynucleotide in conjunction with specific linkers and in conjunction with specific VPM's. But there is no description of how to make the claimed subgenus by the route which is specified in the claims.

In order to arrive at the claimed invention, one must "extract" from the specification a number of different pieces of the puzzle. Not only must one select out combinations of variables (which *combinations* are not described) that determine the structure of the ultimate conjugate, one must also select attempt to glean from the specification those reactants which can produce the final product by the route which is being claimed.

That is one must do the following (in sum):

- a) obtain a  $\text{-CH}_2\text{-O-CH}_2\text{-}$  - containing compound that has at least two branching groups and determine how the compound should be derivatized so as to react with linker groups;
- b ) obtain a "BAM";
- c ) obtain a linker compound, and determine how it should be derivatized so as to react with the  $\text{-CH}_2\text{-O-CH}_2\text{-}$  - containing compound of part (a);
- d ) determine how the compounds of parts (a), (b) and (c) can be reacted to form a conjugate in accordance with instant claim 22.

No doubt applicants will point out that there are a few specific examples of procedures for making specific compounds that fall within the scope of claim 22. But this ground of rejection is directed at the claimed genus, and not merely a few species.

In traversing this ground of rejection, applicants must not only point out the page(s) and line number(s) where descriptive support can be found for the structural description of the final product, but must also point out where descriptive support can be found for the specific route that is recited.

Accordingly, one of skill would conclude that the claimed genus is not described in the specification.



Claims 22 and 32 are rejected under 35 U.S.C. §103 as being unpatentable over Sessler (USP 5,451,576).

Sessler discloses two compounds in figure 11C. Both of these compounds comprise



PEG. Sessler does not disclose that ethyl alcohol is a "BAM".

Though not stated in Sessler, it is well known to the pharmacologist of ordinary skill that ethanol is a "BAM". Aside from its well-known effects on mental function, ethanol is an immunodepressant, a diuretic, an antimicrobial agent, and moreover ethanol affects various receptors including the NMDA receptor, the GABA receptor, and purinergic receptors.

The molecules depicted in figure 11C each comprise four molecules of ethanol. Two of them are bonded to the dimethoxyphenyl group, and the other two are bonded to the end of the PEG group; PEG is itself a polymer of ethyl alcohol. The valency of the molecule is four; the valency is determined not by reactive groups that are present in the claimed molecule, but rather by reactive groups that were present, or could have been present, prior to conjugation of the BAM's to the VPM.

Thus, the claims are rendered obvious.

✦

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



DAVID LUKTON, PH.D.  
PRIMARY EXAMINER